Krishnan
10/517328

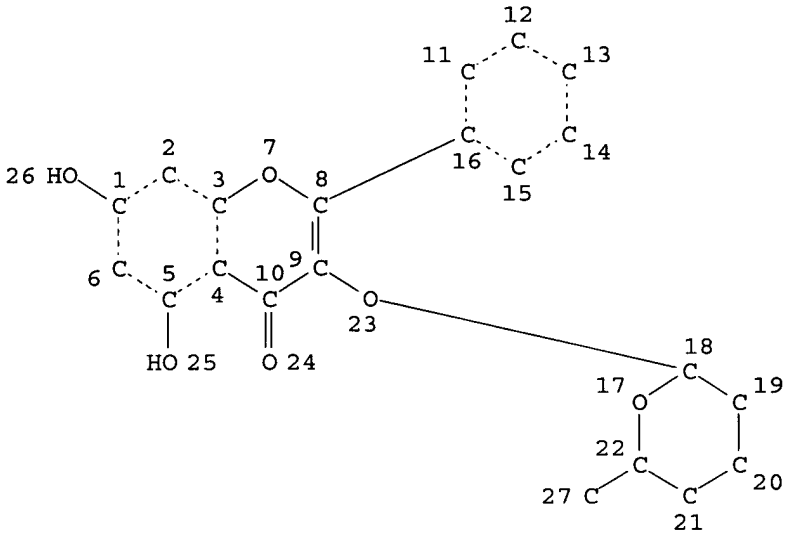
=> dis his

(FILE 'HOME' ENTERED AT 11:56:35 ON 22 NOV 2005)

FILE 'REGISTRY' ENTERED AT 11:56:43 ON 22 NOV 2005

L1 STR
L2 50 S L1
L3 STR L1
L4 50 S L3
L5 1553 S L3 FUL

=> d l5 que stat
L3 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE
L5 1553 SEA FILE=REGISTRY SSS FUL L3

100.0% PROCESSED 3209 ITERATIONS 1553 ANSWERS
SEARCH TIME: 00.00.01

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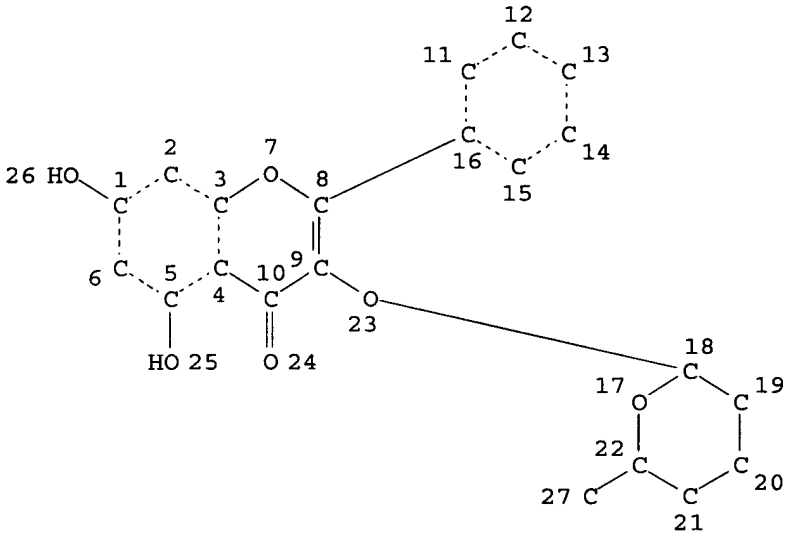
L3 STR

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86



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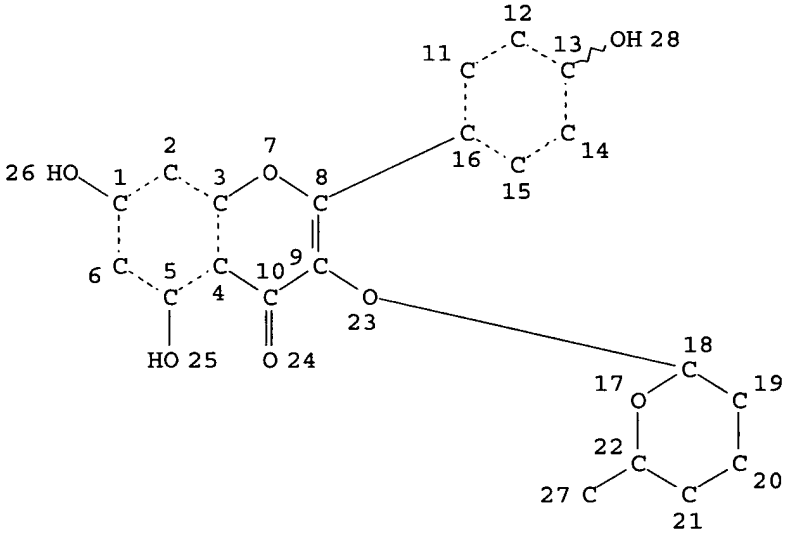
STEREO ATTRIBUTES: NONE
L5 1553 SEA FILE=REGISTRY SSS FUL L3
L6 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L7 1407 SEA FILE=REGISTRY SUB=L5 SSS FUL L6

100.0% PROCESSED 1553 ITERATIONS 1407 ANSWERS
SEARCH TIME: 00.00.01

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	202.82	203.03

FILE 'MEDLINE' ENTERED AT 12:02:18 ON 22 NOV 2005

FILE 'BIOSIS' ENTERED AT 12:02:18 ON 22 NOV 2005

FILE 'EMBASE' ENTERED AT 12:02:18 ON 22 NOV 2005

FILE 'CAPLUS' ENTERED AT 12:02:18 ON 22 NOV 2005

L8 1500 FILE MEDLINE
L9 3176 FILE BIOSIS
L10 2744 FILE EMBASE
L11 12307 FILE CAPLUS

TOTAL FOR ALL FILES
L12 19727 L5

=> s pharm? compos? or compos?
L13 276768 FILE MEDLINE
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L15 238384 FILE EMBASE
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TOTAL FOR ALL FILES
L17 3691110 PHARM? COMPOS? OR COMPOS?

=> s l12 and l17
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L19 300 FILE BIOSIS
L20 148 FILE EMBASE
L21 1740 FILE CAPLUS

TOTAL FOR ALL FILES
L22 2204 L12 AND L17

=> s l22 and rsk
L23 0 FILE MEDLINE
L24 0 FILE BIOSIS
L25 0 FILE EMBASE
L26 1 FILE CAPLUS

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TOTAL FOR ALL FILES
L27 1 L22 AND RSK

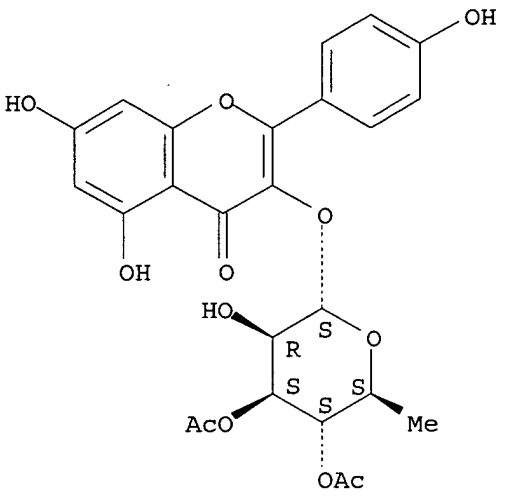
=> d ibib abs hitstr

L27 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1006705 CAPLUS
DOCUMENT NUMBER: 140:53392
TITLE: **Rsk** inhibitors, preparation, and therapeutic uses thereof
INVENTOR(S): Smith, Jeffrey A.; Lannigan-Macara, Deborah A.; Poteet-Smith, Celeste E.; Hecht, Sidney M.; Xu, Yaming; Brautigan, David L.
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105766	A2	20031224	WO 2003-US18734	20030612
WO 2003105766	A3	20040311		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2488864	AA	20031224	CA 2003-2488864	20030612
EP 1539781	A2	20050615	EP 2003-760343	20030612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005233985	A1	20051020	US 2004-517328	20041209

PRIORITY APPLN. INFO.:		
US 2002-388006P	P	20020612
US 2003-449553P	P	20030224
WO 2003-US18734	W	20030612

OTHER SOURCE(S): MARPAT 140:53392
GI



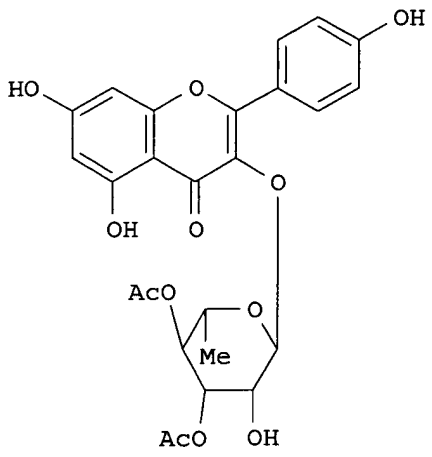
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1006705 CAPLUS
DOCUMENT NUMBER: 140:53392
TITLE: Rsk **inhibitors**, preparation, and **therapeutic** uses thereof
INVENTOR(S): Smith, Jeffrey A.; Lannigan-Macara, Deborah A.; Poteet-Smith, Celeste E.; Hecht, Sidney M.; Xu, Yaming; Brautigan, David L.
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003105766	A2	20031224	WO 2003-US18734		20030612
WO 2003105766	A3	20040311			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2488864	AA	20031224	CA 2003-2488864		20030612
EP 1539781	A2	20050615	EP 2003-760343		20030612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005233985	A1	20051020	US 2004-517328		20041209
PRIORITY APPLN. INFO.:			US 2002-388006P	P	20020612
			US 2003-449553P	P	20030224
			WO 2003-US18734	W	20030612

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

OTHER SOURCE(S): MARPAT 140:53392
GI



I

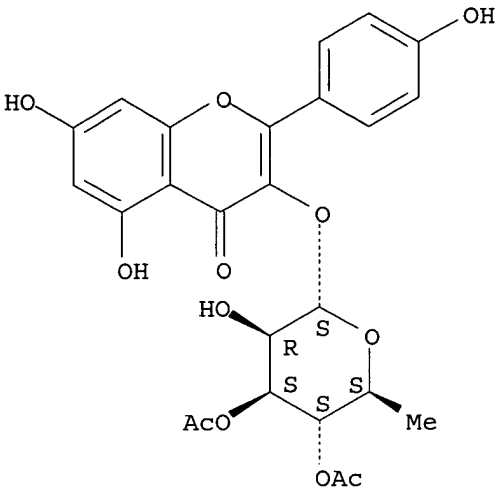
AB The invention discloses compds. and compns. that have Rsk-specific **inhibitory** activity. Compds. of the invention include small mol. **inhibitors**, e.g. I. Synthetic procedures leading to I are described, as are isolation procedures from **Forsteronia refracta.** Other Rsk-specific **inhibitors** include e.g. antisense oligonucleotides. In addition, **inhibition** of Rsk by the compds. has been discovered to halt the proliferation of cancer cell lines while having little effect on the proliferation rate of normal cells. Therefore, the invention identifies Rsk as a target for **therapeutic** intervention in diseased states in which the disease or the symptoms can be ameliorated by **inhibition** of Rsk catalytic activity.

IT **77307-50-7P**, SL 0101-1
RL: DMA (Drug mechanism of action); NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(Rsk **inhibitors** and **therapeutic** uses)

RN 77307-50-7 CAPLUS

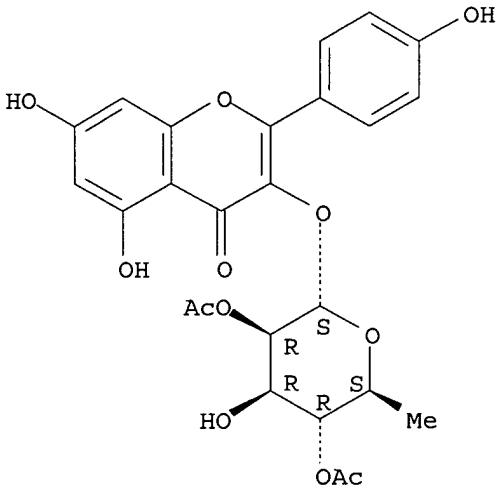
CN 4H-1-Benzopyran-4-one, 3-[(3,4-di-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



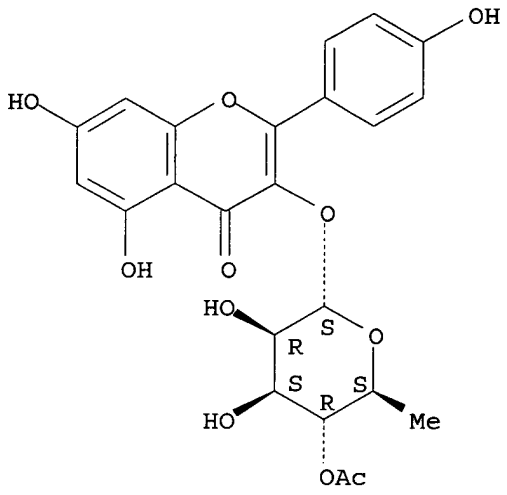
IT **133882-73-2P**, SL 0101-2 **135618-17-6P**, SL 0101-3
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(Rsk **inhibitors** and **therapeutic** uses)
RN 133882-73-2 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(2,4-di-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 135618-17-6 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(4-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



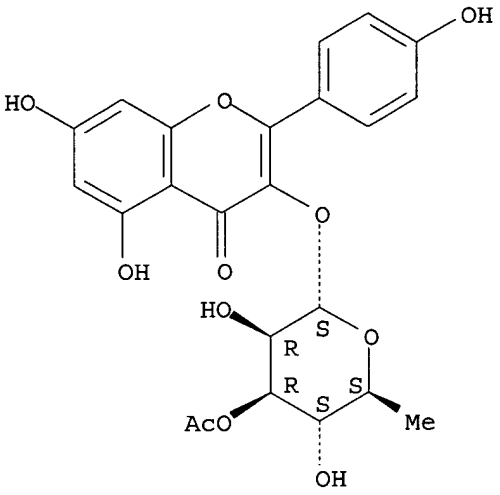
L51 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:429254 CAPLUS
DOCUMENT NUMBER: 127:188240
TITLE: Zerumbone, an HIV-**inhibitory** and cytotoxic sesquiterpene of Zingiber aromaticum and Z. zerumbet
AUTHOR(S): Dai, Jin Rui; Cardellina, John H., II; McMahon, James B.; Boyd, Michael R.
CORPORATE SOURCE: Laboratory Drug Discovery Research Development, National Cancer Institute, Frederick, MD, 21702, USA
SOURCE: Natural Product Letters (1997), 10(2), 115-118
CODEN: NPLEEF; ISSN: 1057-5634
PUBLISHER: Harwood
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Zerumbone and 3",4"-O-diacetylafzelin were isolated from organic exts. of rhizomes of Zingiber aromaticum (Zingiberazeae), and zerumbone and 4"-O-acetylafzelin were obtained from organic exts. of entire plants of Z. zerumbet. Zerumbone exhibited HIV-**inhibitory** and cytotoxic activities, while the afzelins were inactive in both assays.

IT **135618-16-5**, 4"-O-Acetylafzelin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(zerumbone, an HIV-**inhibitory** and cytotoxic sesquiterpene of Zingiber aromaticum and Z. zerumbet)

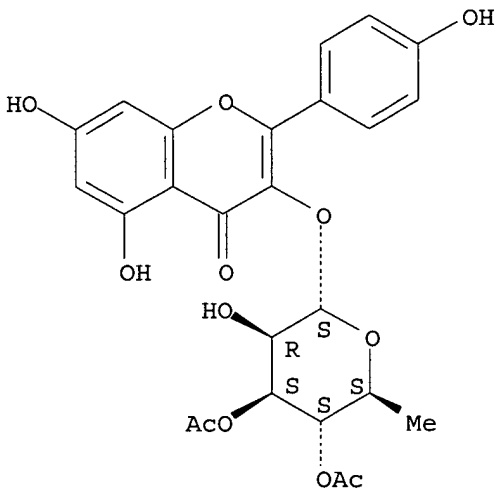
RN 135618-16-5 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(3-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **77307-50-7P**, 3",4"-O-Diacetylafzelin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(zerumbone, an HIV-**inhibitory** and cytotoxic sesquiterpene of Zingiber aromaticum and Z. zerumbet)
RN 77307-50-7 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(3,4-di-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> s (anti tumour or anti tumor or neoplas? or cancer or melanoma) and l36
L52 46 FILE MEDLINE
L53 58 FILE BIOSIS
L54 130 FILE EMBASE
L55 246 FILE CAPLUS

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TOTAL FOR ALL FILES
L56 480 (ANTI TUMOUR OR ANTI TUMOR OR NEOPLAS? OR CANCER OR MELANOMA)
AND L36

=> s p90 ribosomal s6 kinase or ribosomal s6 kinase or serine threonine kinase or
mitogen activate? protein kinase or mapk
L57 51111 FILE MEDLINE
L58 36285 FILE BIOSIS
L59 37372 FILE EMBASE
L60 27187 FILE CAPLUS

TOTAL FOR ALL FILES
L61 151955 P90 RIBOSOMAL S6 KINASE OR RIBOSOMAL S6 KINASE OR SERINE THREONI
NE KINASE OR MITOGEN ACTIVATE? PROTEIN KINASE OR MAPK

=> s l36 and l61
L62 4 FILE MEDLINE
L63 2 FILE BIOSIS
L64 5 FILE EMBASE
L65 5 FILE CAPLUS

TOTAL FOR ALL FILES
L66 16 L36 AND L61

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L67 4 FILE MEDLINE
L68 2 FILE BIOSIS
L69 5 FILE EMBASE
L70 3 FILE CAPLUS

TOTAL FOR ALL FILES
L71 14 L66 NOT (L27 OR L51)

=> dup rem l71
PROCESSING COMPLETED FOR L71
L72 11 DUP REM L71 (3 DUPLICATES REMOVED)

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'HISTR' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files. Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

L73 13544 FILE MEDLINE
L74 16315 FILE BIOSIS
L75 10468 FILE EMBASE
L76 17571 FILE CAPLUS

TOTAL FOR ALL FILES
L77 57898 SMITH J?/AU

L78 0 FILE MEDLINE
L79 0 FILE BIOSIS
L80 0 FILE EMBASE
L81 2 FILE CAPLUS

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TOTAL FOR ALL FILES
L82 2 LANNIGAN MACARA D?/AU

=> d l72 1-11 ibib abs hitstr;s l77 and (l82 or macara d?/au)

L72 ANSWER 1 OF 11 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005252514 EMBASE
TITLE: Quercetin, but not rutin and quercitrin, prevention of H(2)O (2)-induced apoptosis via anti-oxidant activity and heme oxygenase 1 gene expression in macrophages.
AUTHOR: Chow J.-M.; Shen S.-C.; Huan S.K.; Lin H.-Y.; Chen Y.-C.
CORPORATE SOURCE: Y.-C. Chen, Graduate Institute of Pharmacognosy, School of Pharmacy, Taipei Medical University, Taipei, Taiwan,Province of China. yc3270@tmu.edu.tw
SOURCE: Biochemical Pharmacology, (15 Jun 2005) Vol. 69, No. 12, pp. 1839-1851.
Refs: 46
ISSN: 0006-2952 CODEN: BCPCA6
PUBLISHER IDENT.: S 0006-2952(05)00195-4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050707
Last Updated on STN: 20050707

AB In the present study, we examine the protective mechanism of quercetin (QE) on oxidative stress-induced cytotoxic effect in RAW264.7 macrophages. Results of Western blotting show that QE but not its glycoside rutin (RUT) and quicitrin-induced HO-1 protein expression in a time- and dose-dependent manner, and HO-1 protein induced by QE was blocked by an addition of cycloheximide or actinomycin D. Induction of HO-1 gene expression by QE was accompanied by inducing ERKs, but not JNKs or p38, proteins phosphorylation. Addition of PD98059, but not SB203580 or SP600125, significantly attenuates QE-induced HO-1 protein and mRNA expression associated with blocking the expression of phosphorylated ERKs proteins. H(2)O(2) addition reduces the viability of cells by MTT assay, and appearance of DNA ladders, hypodiploid cells, and an increase in intracellular peroxide level was detected. Addition of QE, but not QI or RUT, significantly reduced the cytotoxic effect induced by H(2)O(2) associated with blocking the production of intracellular peroxide, DNA ladders, and hypodiploid cells. QE protection of cells from H(2)O(2)-induced apoptosis was significantly suppressed by adding HO **inhibitor** SnPP or ERKs **inhibitor** PD98059. Additionally, QE protects cells from H(2)O(2)-induced a decrease in the mitochondrial membrane potential and a release of cytochrome c from mitochondria to cytosol by DiOC6 and Western blotting assay, respectively. Activation of apoptotic proteins including the caspase 3, caspase 9, PARP, D4-GDI proteins was identified in H(2)O(2)-**treated** cells by Western blotting and enzyme activity assay, and that was significantly blocked by an addition of QE, but not RUT and QI. Furthermore, HO-1 catalytic metabolites carbon monoxide (CO), but not Fe(2+), Fe(3+), biliverdin or bilirubin, performed protective effect on cells from H(2)O(2)-induced cell death with an increase in HO-1 protein expression and ERKs protein phosphorylation. These data suggest that induction of HO-1 protein may participate in the protective mechanism of QE on oxidative stress (H (2)O(2))-induced apoptosis, and reduction of intracellular ROS production

and mitochondria dysfunction with blocking apoptotic events were involved. Differential anti-apoptotic effect between QE and its glycosides RUT and QI via distinct HO-1 protein induction was also delineated.

L72 ANSWER 2 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1

ACCESSION NUMBER: 2005:283143 BIOSIS
DOCUMENT NUMBER: PREV200510072658
TITLE: **Inhibitors** of the epidermal growth factor receptor in apple juice extract.
AUTHOR(S): Kern, Melanie; Tjaden, Zeina; Ngiewih, Yufanyi; Puppel, Nicole; Will, Frank; Dietrich, Helmut; Pahlke, Gudrun; Marko, Doris [Reprint Author]
CORPORATE SOURCE: Univ Kaiserslautern, Dept Chem, Div Food Chem and Environm Toxicol, Erwin Schroedinger Str 52, D-67663 Kaiserslautern, Germany
marko@rhrk.uni-kl.de
SOURCE: Molecular Nutrition & Food Research, (APR 2005) Vol. 49, No. 4, pp. 317-328.
ISSN: 1613-4125.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005

AB The polyphenol-rich extract of a consumer-relevant apple juice blend was found to potently **inhibit** the growth of the human colon cancer cell line HT29 in vitro. The epidermal growth factor receptor (EGFR) and its subsequent signaling cascade play an important role in the regulation of cell proliferation in HT29 cells. The protein tyrosine kinase activity of an EGFR preparation was effectively **inhibited** by the polyphenol-rich apple juice extract. **Treatment** of intact cells with this extract resulted in the suppression of the subsequent **mitogen-activated protein kinase** cascade. Amongst the so far identified apple juice constituents, the proanthocyanidins B1 and B2 as well as quercetin-3-glc (isoquercitrin) and quercetin-3-gal (hyperoside) were found to possess substantial EGFR-**inhibitory** properties. However, as to be expected from the final concentration of these potential EGFR **inhibitors** in the original polyphenol-rich extract, a synthetic mixture of the apple juice constituents identified and available so far, including both proanthocyanidins and the quercetin glycosides, showed only marginal **inhibitory** effects on the EGFR. These results permit the assumption that yet unknown constituents contribute substantially to the potent EGFR-**inhibitory** properties of polyphenol-rich apple juice extract. In summary, the polyphenol composition of apple juice possesses promising growth-**inhibitory** properties, affecting proliferation-associated signaling cascades in colon tumor cells.

L72 ANSWER 3 OF 11 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2005084568 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15713899
TITLE: Myricetin **inhibits** matrix metalloproteinase 2 protein expression and enzyme activity in colorectal carcinoma cells.
AUTHOR: Ko Ching-Huai; Shen Shing-Chuan; Lee Tony J F; Chen Yen-Chou
CORPORATE SOURCE: Graduate Institute of Pharmaceutical Sciences, School of Pharmacy, 250 Wu-Hsing Street, Taipei, Taiwan.
SOURCE: Molecular cancer therapeutics, (2005 Feb) 4 (2) 281-90.

Journal code: 101132535. ISSN: 1535-7163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 20050217
Last Updated on STN: 20050729
Entered Medline: 20050728

AB Colorectal carcinoma is a leading cause of human mortality due to its high metastatic ability. Because the activation of matrix metalloproteinases (MMP) is a key factor in the metastatic process, agents with the ability to **inhibit** MMP activity have potential in the **treatment** of colorectal carcinoma. In the present study, among 36 flavonoids examined, myricetin was found to be the most potent **inhibitor** of MMP-2 enzyme activity in COLO 205 cells (IC50 = 7.82 micromol/L). Myricetin **inhibition** of MMP-2 enzyme activity was also found in the human colorectal carcinoma cell lines COLO 320HSR, COLO 320DM, HT 29, and COLO 205-X (IC50 = 11.18, 11.56, 13.25, and 23.51 micromol/L, respectively). In contrast, no **inhibitory** effect of MMP-2 protein expression or enzyme activity was observed in myricitrin (myricetin-3-rhamnoside)-**treated** cells. In 12-O-tetradecanoylphorbol-13-acetate (TPA)-stimulated COLO 205 cells, an increase in MMP-2 protein expression and enzyme activity, as well as of protein kinase C (PKC) alpha protein translocation, extracellular signal-regulated kinase (ERK) 1/2 protein phosphorylation, and c-Jun protein expression was observed. ERK **inhibitor** (PD98059) and PKC **inhibitors** (GF-109203X and H-7), but not p38 **inhibitor** (SB203580) or c-jun-NH2-kinase **inhibitor** (SP600125), significantly **inhibited** TPA-induced MMP-2 protein expression, with reduced ERK phosphorylation and c-Jun protein expression. Addition of myricetin but not myricitrin suppressed TPA-induced MMP-2 protein expression in COLO 205 cells by blocking the TPA-induced events, including translocation of PKCalpha from cytosol to membrane, phosphorylation of ERK1/2 protein, and induction of c-Jun protein expression. Addition of PD98059 or GF-109203X significantly enhanced the **inhibitory** effect of myricetin on MMP-2 enzyme activity induced by TPA. Furthermore, myricetin, but not myricitrin, suppressed TPA-induced invasion of COLO 205 cells in an in vitro invasion assay using Engelbreth-Holm-Swarm sarcoma tumor extract Matrigel-coated Transwells. Results of the present study indicate that myricetin significantly blocked both endogenous and TPA-induced MMP-2 enzyme activity by **inhibiting** its protein expression and enzyme activity. The blockade involved suppression of PKC translocation, ERK phosphorylation, and c-Jun protein expression.

L72 ANSWER 4 OF 11 EMBASE

ACCESSION NUMBER: 2004378094 EMBASE
TITLE: Induction of PC12 cell differentiation by flavonoids is dependent upon extracellular signal-regulated kinase activation.
AUTHOR: Sagara Y.; Vanhnasy J.; Maher P.
CORPORATE SOURCE: P. Maher, Department of Cell Biology, Scripps Research Institute, 10550 N. Torrey Pines Road, San Diego, CA 92037, United States. pmaher@scripps.edu
SOURCE: Journal of Neurochemistry, (2004) Vol. 90, No. 5, pp. 1144-1155.
Refs: 42
ISSN: 0022-3042 CODEN: JONRA

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040924
Last Updated on STN: 20040924

AB Many of the physiological benefits attributed to flavonoids are thought to stem from their potent antioxidant and free radical scavenging properties. Recently, it was shown that flavonoids protect nerve cells from oxidative stress by multiple mechanisms, only one of which is directly related to their antioxidant activity, suggesting that specific flavonoids may have other properties that could make them useful in the **treatment** of conditions that lead to nerve cell death. In particular, it was asked if any flavonoid could mimic neurotrophic proteins. To examine this possibility, we looked at the ability of flavonoids to induce nerve cell differentiation using PC12 cells. PC12 cells were **treated** with a variety of flavonoids to determine if there was a correlation between their neuroprotective activity and their neurite outgrowth-promoting activity. In addition, the signaling pathways required for flavonoid-induced differentiation were examined. We found that only a small subset of the flavonoids that were neuroprotective could induce neurite outgrowth by an extracellular signal-regulated kinase-dependent process. There was a strong correlation between the concentrations of the flavonoids that were neuroprotective and the concentrations that induced differentiation. These results suggest that the consumption of specific flavonoids could have further beneficial effects on nerve cells following injury, in pathological conditions or in normal aging.

L72 ANSWER 5 OF 11 MEDLINE on STN
ACCESSION NUMBER: 2005009206 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15635257
TITLE: In vivo modulation of signaling factors involved in cell survival.
AUTHOR: Kumar Mitra Anirban; Krishna Malini
CORPORATE SOURCE: Radiation Biology and Health Sciences Division Bhabha Atomic Research Centre Trombay, Mumbai, India.
SOURCE: Journal of radiation research, (2004 Dec) 45 (4) 491-5. Journal code: 0376611. ISSN: 0449-3060.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050107
Last Updated on STN: 20050513
Entered Medline: 20050512

AB In vivo expression of cell survival factors protein kinase C (PKC), nuclear factor kappaB (NFkappaB), and extracellular signal-regulated kinase (Erk), which may contribute to the development of radioresistance following radiotherapy, was looked for. Their modulation with natural compounds (curcumin, rutin or nicotinamide) was attempted in mice bearing a serially transplanted fibrosarcoma. Expression of protein kinase C was isoform specific. No translocation of any of the isozymes was noticed following gamma-irradiation as has been reported elsewhere. None of the isoforms could be significantly **inhibited** by the modulators. However, significant **inhibition** of radiation-induced ERK and NFkappaB was observed with both curcumin and nicotinamide. Therefore we conclude that use of **inhibitors** of MAP kinases or NFkappaB may

be a more promising strategy to enhance tumour cell killing or to prevent the development of radioresistance during radiotherapy.

L72 ANSWER 6 OF 11 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004034738 EMBASE
TITLE: Nutraceuticals, apoptosis, and disease prevention.
AUTHOR: Gosslau A.; Chen K.Y.
CORPORATE SOURCE: Dr. K.Y. Chen, Dept. of Chem. and Chemical Biology, Rutgers University, Piscataway, NJ 08854-8087, United States. kychen@rutchem.rutgers.edu
SOURCE: Nutrition, (2004) Vol. 20, No. 1, pp. 95-102.
Refs: 143
ISSN: 0899-9007 CODEN: NUTRER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 20040212
Last Updated on STN: 20040212
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L72 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 3

ACCESSION NUMBER: 2003:488158 BIOSIS
DOCUMENT NUMBER: PREV200300489777
TITLE: Tomato and soy polyphenols reduce insulin-like growth factor-I-stimulated rat prostate cancer cell proliferation and apoptotic resistance in vitro via **inhibition** of intracellular signaling pathways involving tyrosine kinase.
AUTHOR(S): Wang, Shihua; DeGroff, Valerie L.; Clinton, Steven K. [Reprint Author]
CORPORATE SOURCE: Division of Hematology and Oncology, Department of Internal Medicine, College of Medicine and Public Health, Ohio State University, Columbus, OH, 43210, USA clinton-1@medctr.osu.edu
SOURCE: Journal of Nutrition, (July 2003) Vol. 133, No. 7, pp. 2367-2376. print.
ISSN: 0022-3166 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Oct 2003
Last Updated on STN: 22 Oct 2003

AB We examined the ability of polyphenols from tomatoes and soy (genistein, quercetin, kaempferol, biochanin A, daidzein and rutin) to modulate insulin-like growth factor-I (IGF-I)-induced in vitro proliferation and apoptotic resistance in the AT6.3 rat prostate cancer cell line. IGF-I at 50 mug/L in serum-free medium produced maximum proliferation and minimized apoptosis. Polyphenols exhibited different abilities to modulate IGF-I-induced proliferation, cell cycle progression (flow cytometry) and apoptosis (Annexin V/propidium iodide and terminal deoxynucleotidyltransferase-mediated deoxyuridine 5'-triphosphate nick end labeling). Genistein, quercetin, kaempferol and biochanin A exhibited dose-dependent **inhibition** of growth with a 50% **inhibitory** concentration (IC50) between 25 and 40 mumol/L, whereas rutin and daidzein were less potent with an IC50 of >60 mumol/L.

Genistein and kaempferol potently induced G2/M cell cycle arrest. Genistein, quercetin, kaempferol and biochanin A, but not daidzein and rutin, counteracted the antiapoptotic effects of IGF-I. Human prostate epithelial cells grown in growth factor-supplemented medium were also sensitive to growth **inhibition** by polyphenols. Genistein, biochanin A, quercetin and kaempferol reduced the insulin receptor substrate-1 (IRS-1) content of AT6.3 cells and prevented the down-regulation of IGF-I receptor beta in response to IGF-I binding. IGF-I-stimulated proliferation was dependent on activation of **mitogen-activated protein kinase** /extracellular signal-regulated kinase (ERK) and phosphatidylinositide 3-kinase pathways. Western blotting demonstrated that ERK1/2 was constitutively phosphorylated in AT6.3 cells with no change in response to IGF-I, whereas IRS-1 and AKT were rapidly and sensitively phosphorylated after IGF-I stimulation. Several polyphenols suppressed phosphorylation of AKT and ERK1/2, and more potently **inhibited** IRS-1 tyrosyl phosphorylation after IGF-I exposure. In summary, polyphenols from soy and tomato products may counteract the ability of IGF-I to stimulate proliferation and prevent apoptosis via **inhibition** of multiple intracellular signaling pathways involving tyrosine kinase activity.

L72 ANSWER 8 OF 11 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003470677 EMBASE
TITLE: Polyphenolic antioxidants **inhibit** peptide presentation by antigen-presenting cells.
AUTHOR: Gong J.; Chen S.-S.
CORPORATE SOURCE: S.-S. Chen, Division of Allergy, La Jolla Inst. for Allerg./Immunol., San Diego, CA, United States. achen@i-genetics.org
SOURCE: International Immunopharmacology, (2003) Vol. 3, No. 13-14, pp. 1841-1852.
Refs: 32
ISSN: 1567-5769 CODEN: IINMBA
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20031204
Last Updated on STN: 20031204

AB Antigen-presenting cells (APC) provide two essential signals, e.g., antigenic peptides as well as costimulatory molecules for T-cell activation. Small molecules of smoke tobacco extracts (SM-STE) **inhibited** antigen presentation of A20 to OVAp-specific T-cell hybridomas. Pretreatment of A20 but not T hybridomas abrogates the APC function. Viability of APC and levels of MHCII, CD40 and B7 of APC were not affected by this **treatment.** The active principle, **inhibiting** APC was reproduced with pure tobacco polyphenols, quercetin and its glycoside, rutin. Antioxidant activity of rutin is relevant since rutin downregulated levels of reactive oxygen species (ROS) in phorbol ester-stimulated A20; moreover, another antioxidant, N-acetyl cysteine (NAC) also **inhibited** antigen presentation, albeit at a higher concentration. Other types of APC, such as bone marrow-derived mast cells (BMMC), MHCII-transfected fibroblast, and splenocytes are affected by tobacco polyphenols. We propose that polyphenols may affect redox-sensitive signal transduction pathway since APC function of PD 98059, MEK **inhibitor**-pretreated A20 were similarly abrogated.

Taken together, we propose that maintaining appropriate intracellular redox of APC is crucial for its antigen-presenting function.

L72 ANSWER 9 OF 11 CAPLUS
ACCESSION NUMBER: 2002:712921 CAPLUS
DOCUMENT NUMBER: 137:242187
TITLE: Neuroprotective effects of **mitogen-activated protein kinase** (**MAPK**) cascade **inhibitors**
INVENTOR(S): Baskys, Andrius
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

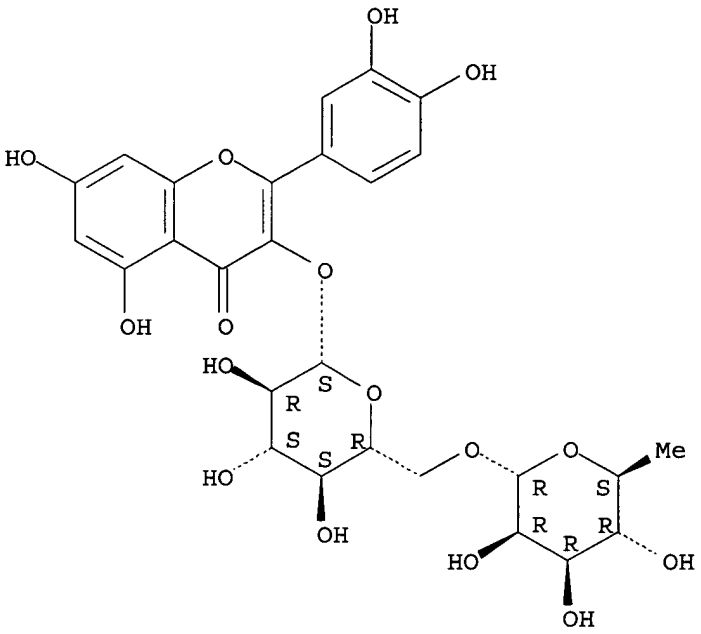
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6451837	B1	20020917	US 2000-653065		20000901
PRIORITY APPLN. INFO.:			US 1999-151955P	P	19990901

AB A method is provided for **therapeutic** use of a class of compds. that are effective in protecting nerve cells from deterioration and cell death arising from degenerative disease, trauma or aging and may be used to achieve a similar effect in male and female subjects with minimal adverse side effects. The method comprises administering a **therapeutically** ED of a natural or synthetic bioflavonoid that acts as an **MAPK** cascade antagonist. Examples of bioflavonoids that may be used in the present method are apigenin and 2-(2'-amino-3' methoxyphenyl)-oxanaphthalen-4-one (PD098059).

IT **153-18-4**, Rutin **482-36-0**, Hyperin **522-12-3**, Quercitrin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective effects of **mitogen-activated protein kinase** (**MAPK**) cascade **inhibitors**)

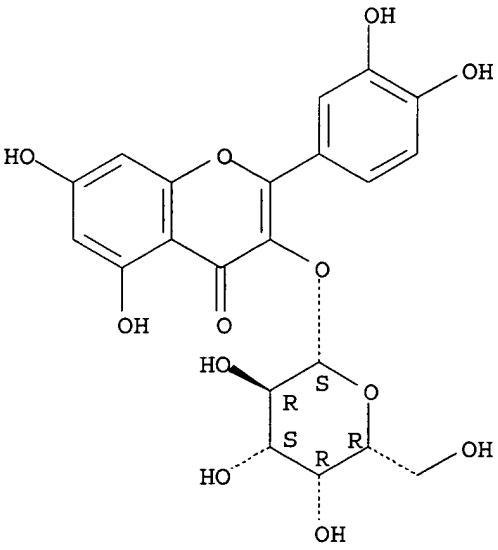
RN 153-18-4 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[[6-O-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



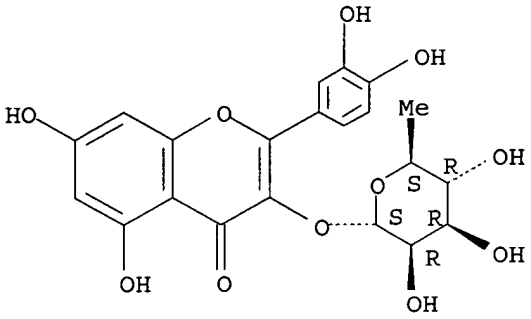
RN 482-36-0 CAPLUS
CN 4H-1-Benzopyran-4-one, 2-(3,4-dihydroxyphenyl)-3-(β-D-galactopyranosyloxy)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 522-12-3 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(6-deoxy-α-L-mannopyranosyl)oxy]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 10 OF 11 MEDLINE on STN
ACCESSION NUMBER: 1999290645 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10363977
TITLE: Competitive and noncompetitive **inhibition** of the DNA-dependent protein kinase.
AUTHOR: Izzard R A; Jackson S P; Smith G C
CORPORATE SOURCE: Wellcome/CRC Institute, Cambridge, United Kingdom.
SOURCE: Cancer research, (1999 Jun 1) 59 (11) 2581-6.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 20021219
Entered Medline: 19990629

AB The DNA-dependent protein kinase (DNA-PK) is a serine/threonine protein kinase that is involved in mammalian DNA double-strand break repair. The catalytic subunit of DNA-PK (DNA-PKcs) shares sequence homology in its kinase domain with phosphatidylinositol (PI) 3-kinase. Here, we provide a detailed kinetic analysis of DNA-PK **inhibition** by the PI 3-kinase **inhibitor** wortmannin and demonstrate this **inhibition** to be of a noncompetitive nature, with a Ki of 120 nM. Another **inhibitor** of PI 3-kinase. LY294002, its parent compound, quercetin, and other derivatives have also been studied. These chemicals are competitive **inhibitors** of DNA-PK, with LY294002 having a Ki of 6.0 microM. Using an antibody to wortmannin, we found that this compound binds covalently to the kinase domain of DNA-PKcs both in vitro and in vivo. Binding of wortmannin to the active site of DNA-PKcs is **inhibited** by ATP but not by a peptide substrate. Furthermore, wortmannin is able to bind to DNA-PKcs independently of Ku, and it is not stimulated by the presence of DNA. This suggests that the ATP binding site of DNA-PKcs is open constitutively and that DNA activation of the kinase is mediated via another mechanism.

L72 ANSWER 11 OF 11 MEDLINE on STN
ACCESSION NUMBER: 95192049 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7885836
TITLE: Promoter control of translation in Xenopus oocytes.
AUTHOR: Gunkel N; Braddock M; Thorburn A M; Muckenthaler M; Kingsman A J; Kingsman S M
CORPORATE SOURCE: EMBL, Heidelberg, Germany.

SOURCE: Nucleic acids research, (1995 Feb 11) 23 (3) 405-12.
Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950425
Last Updated on STN: 20020420
Entered Medline: 19950411

AB The HIV-1 promoter directs the high level production of transcripts in Xenopus oocytes. However, despite being exported to the cytoplasm, the transcripts are not translated [M. Braddock, A. M. Thorburn, A. Chambers, G. D. Elliott, G. J. Anderson, A. J. Kingsman and S. M. Kingsman (1990) Cell, 62, 1123-1133]. We have shown previously that this is a function of promoter sequences and is independent of the TAR RNA element that is normally located at the 5' end of all HIV mRNAs. We now show that a three nucleotide substitution at position -340, upstream of the RNA start site, reverses the translation **inhibition.** This site coincides with a sequence that can bind the haematopoietic transcription factor GATA. The **inhibition** of translation can also be reversed by **treatment** with **inhibitors** of casein kinase II or by injection into the nucleus of antibodies specific for the FRGY2 family of RNP proteins. We suggest that the -340 site influences the quality of the transcription complex such that transcripts are diverted to a nucleus-dependent translation **inhibition** pathway.

L83 0 FILE MEDLINE
L84 0 FILE BIOSIS
L85 0 FILE EMBASE
L86 2 FILE CAPLUS

TOTAL FOR ALL FILES
L87 2 L77 AND (L82 OR MACARA D?/AU)

=> d 1-2 ibib abs hitstr

L87 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:34913 CAPLUS
DOCUMENT NUMBER: 142:132311
TITLE: Kinase ERK7 and ERK8 as novel diagnostic markers for diagnosis of estrogen responsive cancer
INVENTOR(S): **Lannigan-Macara, Deborah A.**; Henrich, Lorin M.; **Smith, Jeffrey A.**
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003371	A2	20050113	WO 2004-US19181	20040617
WO 2005003371	A3	20050428		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-478992P P 20030617

AB The present invention is directed in part to the discovery of a novel signal transduction pathway that regulates estrogen responsiveness. Human extracellular signal-regulated kinase 8 (ERK8) has been discovered by applicants to preferentially enhance the destruction of ERα, and loss of ERK8 is correlated with breast cancer progression. Thus monitoring the expression of ERK8 can be used as a diagnostic and therapeutic indicator of cancer and cancer progression. ERK7 specifically enhanced ERα degrdn and ERK7 regulation of ERa degradation rate is important in determining estrogen responsiveness. Although ERK7 may enhance Ser-118 phosphorylation it seems that mechanisms other than ERa phosphorylation are important in targeting ERa for destruction. The invention provides the protein sequence of human ERK8.

L87 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1006705 CAPLUS
DOCUMENT NUMBER: 140:53392
TITLE: Rsk inhibitors, preparation, and therapeutic uses thereof
INVENTOR(S): **Smith, Jeffrey A.**; **Lannigan-Macara, Deborah A.**; Poteet-Smith, Celeste E.; Hecht, Sidney M.; Xu, Yaming; Brautigan, David L.
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003105766	A2	20031224	WO 2003-US18734	20030612
WO 2003105766	A3	20040311		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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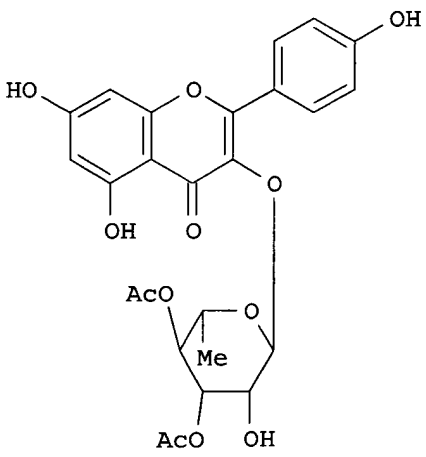
EP 1539781	A2	20050615	EP 2003-760343	20030612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005233985	A1	20051020	US 2004-517328	20041209

PRIORITY APPLN. INFO.: US 2002-388006P P 20020612

US 2003-449553P P 20030224
WO 2003-US18734 W 20030612

OTHER SOURCE(S): MARPAT 140:53392
GI



I

AB The invention discloses compds. and compns. that have Rsk-specific inhibitory activity. Compds. of the invention include small mol. inhibitors, e.g. I. Synthetic procedures leading to I are described, as are isolation procedures from Forsteronia refracta. Other Rsk-specific inhibitors include e.g. antisense oligonucleotides. In addition, inhibition of Rsk by the compds. has been discovered to halt the proliferation of cancer cell lines while having little effect on the proliferation rate of normal cells. Therefore, the invention identifies Rsk as a target for therapeutic intervention in diseased states in which the disease or the symptoms can be ameliorated by inhibition of Rsk catalytic activity.

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FILE 'REGISTRY' ENTERED AT 11:56:43 ON 22 NOV 2005
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L5 1553 S L3 FUL
L6 STR L3
L7 1407 SEARCH L6 SUB=L5 FUL

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L14 518133 FILE BIOSIS
L15 238384 FILE EMBASE

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L48            0 FILE BIOSIS
L49            0 FILE EMBASE
L50            3 FILE CAPLUS
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L51            3 S L36 AND L46
L52           46 FILE MEDLINE
L53           58 FILE BIOSIS
L54          130 FILE EMBASE
L55          246 FILE CAPLUS
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L56          480 S (ANTI TUMOUR OR ANTI TUMOR OR NEOPLAS? OR CANCER OR MELANOMA)
L57        51111 FILE MEDLINE
L58        36285 FILE BIOSIS
L59        37372 FILE EMBASE
L60        27187 FILE CAPLUS
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L62            4 FILE MEDLINE
L63            2 FILE BIOSIS
L64            5 FILE EMBASE
L65            5 FILE CAPLUS
     TOTAL FOR ALL FILES
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
L66           16 S L36 AND L61
L67            4 FILE MEDLINE
L68            2 FILE BIOSIS
L69            5 FILE EMBASE
L70            3 FILE CAPLUS
     TOTAL FOR ALL FILES
L71           14 S L66 NOT (L27 OR L51)
L72           11 DUP REM L71 (3 DUPLICATES REMOVED)
L73        13544 FILE MEDLINE
L74        16315 FILE BIOSIS
L75        10468 FILE EMBASE
L76        17571 FILE CAPLUS
     TOTAL FOR ALL FILES
L77        57898 S SMITH J?/AU
L78            0 FILE MEDLINE
L79            0 FILE BIOSIS
L80            0 FILE EMBASE
L81            2 FILE CAPLUS
     TOTAL FOR ALL FILES
L82            2 S LANNIGAN MACARA D?/AU
L83            0 FILE MEDLINE
L84            0 FILE BIOSIS
L85            0 FILE EMBASE
L86            2 FILE CAPLUS
     TOTAL FOR ALL FILES
L87            2 S L77 AND (L82 OR MACARA D?/AU)

=> d l5 que stat
L3               STR
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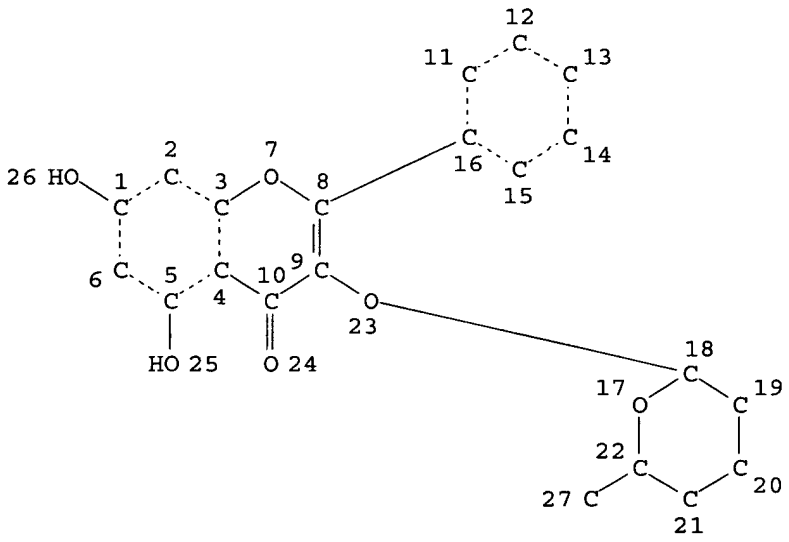


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  27

STEREO ATTRIBUTES: NONE
L5          1553 SEA FILE=REGISTRY SSS FUL L3


Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
```

100.0% PROCESSED 3209 ITERATIONS 1553 ANSWERS
SEARCH TIME: 00.00.01

=> s l5 and (l82 or l77 or macara d?/au)
L88 0 FILE MEDLINE
L89 0 FILE BIOSIS
L90 0 FILE EMBASE
L91 2 FILE CAPLUS

TOTAL FOR ALL FILES
L92 2 L5 AND (L82 OR L77 OR MACARA D?/AU)

=> s l92 not l87
L93 0 FILE MEDLINE
L94 0 FILE BIOSIS
L95 0 FILE EMBASE
L96 1 FILE CAPLUS

TOTAL FOR ALL FILES
L97 1 L92 NOT L87

=> d ibib abs hitstr

L97 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:101479 CAPLUS
DOCUMENT NUMBER: 142:329195
TITLE: Identification of the first specific inhibitor of p90 ribosomal S6 kinase (RSK) reveals an unexpected role for RSK in cancer cell proliferation
AUTHOR(S): **Smith, Jeffrey A.**; Poteet-Smith, Celeste E.; Xu, Yaming; Errington, Timothy M.; Hecht, Sidney M.; Lannigan, Deborah A.
CORPORATE SOURCE: Center for Cell Signaling, University of Virginia, Charlottesville, VA, USA
SOURCE: Cancer Research (2005), 65(3), 1027-1034
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB P90 ribosomal S6 kinase (RSK) is an important downstream effector of mitogen-activated protein kinase, but its biol. functions are not well understood. The authors have now identified the first small-mol., RSK-specific inhibitor, which they isolated from the tropical plant Forsteronia refracta. The authors have named this novel inhibitor SL0101. SL0101 shows remarkable specificity for RSK. The major determinant of SL0101-binding specificity is the unique ATP-interacting sequence in the amino-terminal kinase domain of RSK. SL0101 inhibits proliferation of the human breast cancer cell line MCF-7, producing a cell cycle block in G1 phase with an efficacy paralleling its ability to inhibit RSK in intact cells. RNA interference of RSK expression confirmed that RSK regulates MCF-7 proliferation. Interestingly, SL0101 does not alter proliferation of a normal human breast cell line MCF-10A, although SL0101 inhibits RSK in these cells. RSK is overexpressed in .apprx. 50% of human breast cancer tissue samples, suggesting that regulation of RSK has been compromised. Thus, RSK has an unexpected role in proliferation of transformed cells and may be a useful new target for chemotherapeutic agents. SL0101 will provide a powerful new tool to dissect the mol.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

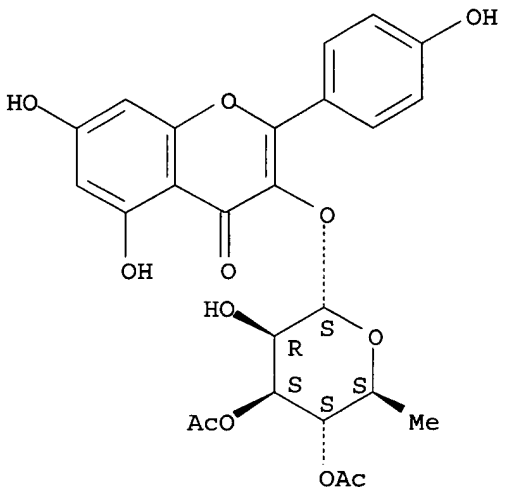
functions of RSK in cancer cells.

IT **77307-50-7**
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(identification of first specific inhibitor of p90 ribosomal S6 kinase (RSK) reveals an unexpected role for RSK in cancer cell proliferation)

RN 77307-50-7 CAPLUS

CN 4H-1-Benzopyran-4-one, 3-[(3,4-di-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his

(FILE 'HOME' ENTERED AT 11:56:35 ON 22 NOV 2005)

FILE 'REGISTRY' ENTERED AT 11:56:43 ON 22 NOV 2005

L1		STR
L2	50	S L1
L3		STR L1
L4	50	S L3
L5	1553	S L3 FUL
L6		STR L3
L7	1407	SEARCH L6 SUB=L5 FUL

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 12:02:18 ON 22 NOV 2005

L8	1500	FILE MEDLINE
L9	3176	FILE BIOSIS
L10	2744	FILE EMBASE
L11	12307	FILE CAPLUS
TOTAL FOR ALL FILES		
L12	19727	S L5
L13	276768	FILE MEDLINE
L14	518133	FILE BIOSIS
L15	238384	FILE EMBASE
L16	2657825	FILE CAPLUS

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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     TOTAL FOR ALL FILES
L17     3691110 S PHARM? COMPOS? OR COMPOS?
L18          16 FILE MEDLINE
L19         300 FILE BIOSIS
L20         148 FILE EMBASE
L21        1740 FILE CAPLUS
     TOTAL FOR ALL FILES
L22        2204 S L12 AND L17
L23           0 FILE MEDLINE
L24           0 FILE BIOSIS
L25           0 FILE EMBASE
L26           1 FILE CAPLUS
     TOTAL FOR ALL FILES
L27           1 S L22 AND RSK
L28     4653890 FILE MEDLINE
L29     3541114 FILE BIOSIS
L30     4235684 FILE EMBASE
L31     4773546 FILE CAPLUS
L32         869 FILE MEDLINE
L33         782 FILE BIOSIS
L34        1208 FILE EMBASE
L35        3182 FILE CAPLUS
     TOTAL FOR ALL FILES
L36        6041 S L12 AND (THERAP? OR TREAT? OR INHIBIT?)
L37           0 FILE MEDLINE
L38           0 FILE BIOSIS
L39           0 FILE EMBASE
L40           0 FILE CAPLUS
     TOTAL FOR ALL FILES
L41           0 S RSK! AND L36
L42          14 FILE MEDLINE
L43          46 FILE BIOSIS
L44          14 FILE EMBASE
L45          74 FILE CAPLUS
     TOTAL FOR ALL FILES
L46         148 S FORSTERONIA REFRACTA OR ZINGIBER ZERUMBET
L47           0 FILE MEDLINE
L48           0 FILE BIOSIS
L49           0 FILE EMBASE
L50           3 FILE CAPLUS
     TOTAL FOR ALL FILES
L51           3 S L36 AND L46
L52          46 FILE MEDLINE
L53          58 FILE BIOSIS
L54         130 FILE EMBASE
L55         246 FILE CAPLUS
     TOTAL FOR ALL FILES
L56         480 S (ANTI TUMOUR OR ANTI TUMOR OR NEOPLAS? OR CANCER OR MELANOMA)
L57       51111 FILE MEDLINE
L58       36285 FILE BIOSIS
L59       37372 FILE EMBASE
L60       27187 FILE CAPLUS
     TOTAL FOR ALL FILES
L61      151955 S P90 RIBOSOMAL S6 KINASE OR RIBOSOMAL S6 KINASE OR SERINE THRE
L62           4 FILE MEDLINE
L63           2 FILE BIOSIS
L64           5 FILE EMBASE
L65           5 FILE CAPLUS
     TOTAL FOR ALL FILES
L66          16 S L36 AND L61
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```
L67             4 FILE MEDLINE
L68             2 FILE BIOSIS
L69             5 FILE EMBASE
L70             3 FILE CAPLUS
     TOTAL FOR ALL FILES
L71            14 S L66 NOT (L27 OR L51)
L72            11 DUP REM L71 (3 DUPLICATES REMOVED)
L73         13544 FILE MEDLINE
L74         16315 FILE BIOSIS
L75         10468 FILE EMBASE
L76         17571 FILE CAPLUS
     TOTAL FOR ALL FILES
L77         57898 S SMITH J?/AU
L78             0 FILE MEDLINE
L79             0 FILE BIOSIS
L80             0 FILE EMBASE
L81             2 FILE CAPLUS
     TOTAL FOR ALL FILES
L82             2 S LANNIGAN MACARA D?/AU
L83             0 FILE MEDLINE
L84             0 FILE BIOSIS
L85             0 FILE EMBASE
L86             2 FILE CAPLUS
     TOTAL FOR ALL FILES
L87             2 S L77 AND (L82 OR MACARA D?/AU)
L88             0 FILE MEDLINE
L89             0 FILE BIOSIS
L90             0 FILE EMBASE
L91             2 FILE CAPLUS
     TOTAL FOR ALL FILES
L92             2 S L5 AND (L82 OR L77 OR MACARA D?/AU)
L93             0 FILE MEDLINE
L94             0 FILE BIOSIS
L95             0 FILE EMBASE
L96             1 FILE CAPLUS
     TOTAL FOR ALL FILES
L97             1 S L92 NOT L87

=> log y

COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               328.59     531.62

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -5.84      -5.84

STN INTERNATIONAL LOGOFF AT 12:11:44 ON 22 NOV 2005
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CS ST XAVIER COLL, DEPT BOT, PALAYANKOTTAI 627002, TAMIL NADU, INDIA; MANONMANIAN SUNDRAMAR UNIV, DEPT CHEM, PALAYANKOTTAI, TAMIL NADU 6270, INDIA; SCI UNIV TOKYO, FAC PHARMACEUT SCI, SHINJUKU KU, TOKYO 162, JAPAN
CYA INDIA; JAPAN
SO CHEMICAL & PHARMACEUTICAL BULLETIN, (OCT 1995) Vol. 43, No. 10, pp. 1800-1803.
ISSN: 0009-2363.
PB PHARMACEUTICAL SOC JAPAN, 2-12-15-201 SHIBUYA, SHIBUYA-KU, TOKYO 150, JAPAN.
DT Note; Journal
FS LIFE
LA English
REC Reference Count: 8
ED Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Clerodane glycosides and flavonoids in Dicranopteris pedata and three varieties of D. linearis were investigated. All the ferns contained a new glycoside, (6S,13S)-6-[6-O-**acetyl**-beta-D-glucopyranosyl-(1-->4)-alpha-L-rhamnopyranosyloxy] -13-[alpha-L-rhamnopyranosyl-(1-->4)-beta-D-fucopyranosyloxy]-cleroda-3,14-diene, as a chemical marker of this group, Flavonoids were limited to flavonol 3-O-glycosides. The ferns and isolated flavonoids are as follows; D. pedata: **afzelin**, quercitrin, D. linear is var, brevis: **afzelin**, quercitrin. D. linearis var, tenuis: quercitrin, isoquercitrin. D. linearis var, sebastiana: astragarin, isoquercitrin, rutin, kaempferol 3-O-(4-O-p-coumaroyl-3-O-alpha-L-rhamnopyranosyl)-alpha-L-rhamnopyranosyl-(1-->6)-beta-D-glucopyranoside.

L2 ANSWER 16 OF 23 WPINDEX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2005-546353 [56] WPINDEX
DNC C2005-165620
TI Composition for treating malaria caused by Plasmodium, contains flavonoid mono-glycoside or its salt as active ingredient.
DC B04
IN HORII, T; KUBATA, B K; MURAKAMI, K; TAMURA, O; URADE, Y
PA (SANE-N) SANEIGEN FFI KK
CYC 1
PI JP 2005206500 A 20050804 (200556)* 22
ADT JP 2005206500 A JP 2004-13675 20040121
PRAI JP 2004-13675 20040121
AN 2005-546353 [56] WPINDEX
AB JP2005206500 A UPAB: 20050902
NOVELTY - Anti-malaria composition containing flavonoid mono-glycoside (1) or its salt as an active ingredient, is new.
DETAILED DESCRIPTION - Anti-malaria composition containing flavonoid mono-glycoside of formula (1) or its salt as an active ingredient.
R1,R2=H, hydroxyl, lower **alkoxy**, -OCOR9, -OCOOR9 or -OCONHR9;
R9=lower alkyl;and
R3-R8=H, lower alkyl, acyl, lower alkoxycarbonyl or lower alkyl carbamoyl.
An INDEPENDENT CLAIM is also included for method for preparing anti-malaria composition, which involves mixing flavonoid mono-glycoside (1) or its salt as an active ingredient with carrier or additive.
ACTIVITY - Antimalarial.
The ability of ethyl acetate extract of Euphorbia hirta (5 mu g/ml) to inhibit the growth of Plasmodium falciparum was tested. The extract was found to have growth inhibition rate of 87.7%.
MECHANISM OF ACTION - None given.
USE - For treating malaria caused by Plasmodium.
ADVANTAGE - The composition is excellent in treating malaria.
Dwg.0/0

L2 ANSWER 17 OF 23 MEDLINE on STN
AN 2003212106 MEDLINE
DN PubMed ID: 12713413
TI Phenolic compounds from Nymphaea odorata.
AU Zhang Zhizhen; ElSohly Hala N; Li Xing-Cong; Khan Shabana I; Broedel

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Sheldon E Jr; Raulli Robert E; Cihlar Ronald L; Burandt Charles; Walker Larry A
CS National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, and Department of Pharmacology, School of Pharmacy, University of Mississippi, University, Mississippi 38677, USA.
NC 5 R01 CA88456-02 (NCI)
SO Journal of natural products, (2003 Apr) 66 (4) 548-50.
Journal code: 7906882. ISSN: 0163-3864.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030508
Last Updated on STN: 20031003
Entered Medline: 20031002
AB Assay-guided fractionation of the ethanol extract of Nymphaea odorata resulted in the identification of two lignans, one new (1) and one known (2), together with six known flavonol glycosides (3-8). The structures of 1-8 were established by spectroscopic analysis as nymphaeoside A (1), icariside E(4) (2), kaempferol 3-O-alpha-l-rhamnopyranoside (**afzelin**, 3), quercetin 3-O-alpha-l-rhamnopyranoside (4), myricetin 3-O-alpha-l-rhamnopyranoside (myricitrin, 5), quercetin 3-O-(6' '-O-**acetyl**)-beta-d-galactopyranoside (6), myricetin 3-O-beta-d-galactopyranoside (7), and myricetin 3-O-(6' '-O-**acetyl**)-beta-d-galactopyranoside (8). Compounds 3, 4, and 7 showed marginal inhibitory effect against fatty acid synthase with IC(50) values of 45, 50, and 25 microg/mL, respectively.

L2 ANSWER 18 OF 23 MEDLINE on STN
AN 96076695 MEDLINE
DN PubMed ID: 8536353
TI Chemical and chemotaxonomical studies on Dicranopteris species.
AU Raja D P; Manickam V S; de Britto A J; Gopalakrishnan S; Ushioda T; Satoh M; Tanimura A; Fuchino H; Tanaka N
CS Department of Botany, St. Xavier's College, Tamil Nadu, India.
SO Chemical & pharmaceutical bulletin, (1995 Oct) 43 (10) 1800-3.
Journal code: 0377775. ISSN: 0009-2363.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199602
ED Entered STN: 19960221
Last Updated on STN: 19960221
Entered Medline: 19960208
AB Clerodane glycosides and flavonoids in Dicranopteris pedata and three varieties of D. linearis were investigated. All the ferns contained a new glycoside, (6S,13S)-6-[6-O-**acetyl**-beta-D-glucopyranosyl-(1-->4)-alpha-L-rhamnopy - ranosyloxy]-13-[alpha-L-rhamnopyranosyl-(1-->4)-beta-D-fucopyra nosyloxy]- cleroda-3,14-diene, as a chemical marker of this group. Flavonoids were limited to flavonol 3-O-glycosides. The ferns and isolated flavonoids are as follows; D. pedata: **afzelin**, quercitrin. D. linearis var. brevis: **afzelin**, quercitrin. D. linearis var. tenuis: quercitrin, isoquercitrin. D. linearis var. sebastiana: astragarin, isoquercitrin, rutin, kaempferol 3-O-(4-O-p-coumaroyl-3-O-alpha-L-rhamnopyranosyl)-alpha-L-rhamn opy ranosyl- (1-->6)-beta-D-glucopyranoside.

L2 ANSWER 19 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1996:31920 BIOSIS
DN PREV199698604055
TI Chemical and chemotaxonomical studies on Dicranopteris species.
AU Raja, Diraviam Patric; Manickam, Visuvasam Soosai; De Britto, Alexis John; Gopalakrishnan, Subarayan; Ushioda, Toshiyuki; Satoh, Masako; Tanimura, Akinobu; Fuchino, Hiroyuki; Tanaka, Nobutoshi [Reprint author]
CS Fac. Pharm. Sci., Sci. Univ. Tokyo, Funakawara-machi, Ichigaya, Shinjuku-ku, Tokyho 162, Japan

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SO Chemical and Pharmaceutical Bulletin (Tokyo), (1995) Vol. 43, No. 10, pp. 1800-1803.
CODEN: CPBTAL. ISSN: 0009-2363.
DT Article
LA English
ED Entered STN: 26 Jan 1996
Last Updated on STN: 26 Jan 1996
AB Clerodane glycosides and flavonoids in Dicranopteris pedata and three varieties of D. linearis were investigated. All the ferns contained a new glycoside, (6S,13S)-6-(6-O-**acetyl**-beta-D-glucopyranosyl-(1 fwdarw 4)-alpha-L-rhamnopyranosyloxy)-13-(alpha-L-rhamnopyranosyl-(1 fwdarw 4)-beta-D-fucopyranosyloxy)-cleroda-3,14-diene, as a chemical marker of this group. Flavonoids were limited to flavonol 3-O-glycosides. The ferns and isolated flavonoids are as follows; D. pedata: **afzelin**, quercitrin. D. linearis var. brevis: **afzelin**, quercitrin. D. linearis var. tenuis: quercitrin, isoquercitrin. D. linearis var. sebastiana: astragarin, isoquercitrin, rutin, kaempferol 3-O-(4-O-p-coumaroyl-3-O-alpha-L-rhamnopyranosyl)-alpha-L-rhamnopyranosyl-(1 fwdarw 6)-beta-D-glucopyranoside.

L2 ANSWER 20 OF 23 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1980:129930 BIOSIS
DN PREV198069004926; BA69:4926
TI THE PURGATIVE DRUGS 5. THE CONSTITUENTS OF THE FRUITS OF PRUNUS-JAPONICA.
AU TAKAGI S [Reprint author]; YAMAKI M; MASUDA K; INOUE K; KASE Y
CS FAC PHARM SCI, MUKAGAWA WOMEN'S UNIV, 4-16 EDAGAWA, NISHINOMIYA, HYOGO, JPN
SO Yakugaku Zasshi, (1979) Vol. 99, No. 4, pp. 439-442.
CODEN: YKKZAJ. ISSN: 0031-6903.
DT Article
FS BA
LA JAPANESE
AB Prunuside from purgative drugs, the fruits of P. japonica Thunb. was identified with multiflorin A [kaempferol-3-(6-O-**acetyl**)-β-D-glucopyranosyl-(1 → 4)-α-L-rhamnopyranoside]. In addition, 3 compounds, ursolic acid, vanillic acid, protocatechuic acid and 4 known flavonoids, **afzelin**, kaempferitrin, multiflorin B(VII) and multinoside A were isolated.

L2 ANSWER 21 OF 23 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2005032752 EMBASE
TI [HPLC investigation of antioxidant components in Solidaginis herba]. SOLIDAGO FAJOK ANTIOXIDANS HATOANYAGAINAK HPLC VIZSGALATA.
AU Apati P.; Houghton P.J.; Kery A.
CS P. Apati, Semmelweis Egyetem, Farmakognozia Intezet, Ulloi ut 26, Budapest, H - 1085, Hungary
SO Acta Pharmaceutica Hungarica, (2004) Vol. 74, No. 4, pp. 223-231.
Refs: 19
ISSN: 0001-6659 CODEN: APHGAO
CY Hungary
DT Journal; Article
FS 030 Pharmacology
037 Drug Literature Index
LA Hungarian
SL English; Hungarian
ED Entered STN: 20050204
Last Updated on STN: 20050204
AB Representatives of Solidago species have been used in European phytotheraphy for centuries as a component of urological and antiphlogistical remedies. Solidago canadensis L. (Asteraceae) contains a wide range of active ingredients, such as flavonoids, saponins, hydroxycinnamates and mineral elements, which are responsible for its characteristic anti-inflammatory, spasmolytic and diuretic properties. Quality control of collected Solidaginis herba were performed according to the instructions of the X. German Pharmacopoea, while different LC-MS technologies were applied to evaluate the exact phenoloid composition. Three flavonol aglycons (quercetin, kaempferol and isorhamnetin) connected

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to several sugar components (glucose, rhamnose, galactose and rutinose), caffeoylcjuinic acid and a caffeoyl-shikimic acid glycoside were identified in the samples. Quercetin-3-O-β-glucoside (isoquercitrin), quercetin-3-O-β-galactoside (hyperoside), quercetin-3-O-β-rhamnoside (quercitrin), quercetin-3-O-β-rutinoside (rutin), kaempferol-3-O-β-rhamnoside (**afzelin**), kaempferol-3-O-β- rutinoside (nicotiflorin), caffeoil-quinic acid (chlorogenic acid) were identified in sample "A", while the presence of quercetin, quercetin-3-O-β-glucoside (isoquercitrin), quercetin-3-/6"-O-**acetyl**-/ -β-glucopiranoside, quercetin-3-O-β-rutinoside (rutin), kaempferol, kaempferol-3-O-β-glucoside (astragalin), kaempferol-3-/6"-O-**acetyl**-/-β-glucopiranoside, isorhamnetin, isorhamnetin-3-/6"-O- **acetyl** -/- β-glucopiranoside, isorhamnetin-3-O-β-rutinoside (narcissin), caffeoil-quinic acid (chlorogenic acid), caffeoil-shikimic acid-glucoside (dattelic acid-glucoside) were confirmed in sample "B". According to the occurrence of **acetyl**-glycosides and the diversity of sugar component of flavonoid glycosides Solidaginis herba samples chemotaxonomically were classified into different varieties. Incidence of **acetyl**-glycosidic flavonoids and absence of flavonoid galactosides and rhamnosides in the sample "B" together give support for the taxonomic recognition of varietases Solidago canadensis L. var. canadensis and var. scabra. Sample "A" was identified as Solidago canadensis L. var. canadensis, while sample "B" has proved to be belong to variety Solidago canadensis L. var. scabra. Due to the same flavonoid aglycons and the large amounts of flavonol glycosides occurring in each drug, phytochemical characteristics of investigated samples proved to be very similar.

L2 ANSWER 22 OF 23 EMBASE
AN 2003181303 EMBASE
TI Phenolic compounds from Nymphaea odorata.
AU Zhang Z.; ElSohly H.N.; Li X.-C.; Khan S.I.; Broedel Jr. S.E.; Raulli R.E.; Cihlar R.L.; Burandt C.; Walker L.A.
CS H.N. ElSohly, Natl. Ctr. for Nat. Prod. Research, Res. Inst. of Pharmaceut. Sciences, University of Mississippi, University, MS 38677, United States. helsohly@olemiss.edu
SO Journal of Natural Products, (1 Apr 2003) Vol. 66, No. 4, pp. 548-550. Refs: 15
ISSN: 0163-3864 CODEN: JNPRDF
CY United States
DT Journal; Article
FS 037 Drug Literature Index
LA English
SL English
ED Entered STN: 20030522
Last Updated on STN: 20030522
AB Assay-guided fractionation of the ethanol extract of Nymphaea odorata resulted in the identification of two lignans, one new (1) and one known (2), together with six known flavonol glycosides (3-8). The structures of 1-8 were established by spectroscopic analysis as nymphaeoside A (1), icariside E(4) (2), kaempferol 3-O-α-L-rhamnopyranoside (**afzelin**, 3), quercetin 3-O-α-L-rhamnopyranoside (4), myricetin 3-O-α-L-rhamnopyranoside (myricitrin, 5), quercetin 3-O-(6"-O-**acetyl**)-β-D-galactopyranoside (6), myricetin 3-O-β-D-galactopyranoside (7), and myricetin 3-O-(6"-O- **acetyl**)-β-D-galactopyranoside (8). Compounds 3, 4, and 7 showed marginal inhibitory effect against fatty acid synthase with IC(50) values of 45, 50, and 25 μg/mL, respectively.

L2 ANSWER 23 OF 23 EMBASE
AN 95340247 EMBASE
DN 1995340247
TI Chemical and chemotaxonomical studies on Dicranopteris species.
AU Raja D.P.; Manickam V.S.; De Britto A.J.; Gopalakrishnan S.; Ushioda T.; Satoh M.; Tanimura A.; Fuchino H.; Tanaka N.
CS Faculty of Pharmaceutical Sciences, Science University of Tokyo,

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Funakawara-machi, Ichigaya,Shinjuku-ku, Tokyo 162, Japan
SO Chemical and Pharmaceutical Bulletin, (1995) Vol. 43, No. 10, pp. 1800-1803.
ISSN: 0009-2363 CODEN: CPBTAL
CY Japan
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
ED Entered STN: 951205
Last Updated on STN: 951205
AB Clerodane glycosides and flavonoids in Dicranopteris pedata and three varieties of D. linearis were investigated. All the ferns contained a new glycoside, (6S, 13s)-6-[6-O-**acetyl**-β-D-glucopyranosyl-(1→4)-α-L- rhamnopyranosyloxy]-13-[α-L-rhamnopyranosyl→4)-β-D-fucopyranosyloxy]- cleroda-3,14-diene, as a chemical marker of this group. Flavonoids were limited to flavonol 3-O-glycosides. The ferns and isolated flavonoids are as follows; D. pedata: **afzelin**, quercitrin. D. linearis var. brevis: **afzelin**, quercitrin. D. linearis var. tennis: quercitrin, isoquercitrin. D. linearis var. sebastiana: astragarin, isoquercitrin, rutin, kaempferol 3-O-(4-O-p- coumaroyl-3-O-α-L-rhamnopyranosyl)-α-L-rhamnopyranosyl-(1→6)-β-D- glucopyranoside.

=> s kaempferol
20 FILES SEARCHED...
L3 16275 KAEMPFEROL

=> s l3 and (acetyl(s)rhamnopyranosyl)
15 FILES SEARCHED...
L4 62 L3 AND (ACETYL(S) RHAMNOPYRANOSYL)

=> s l4 and treat?
18 FILES SEARCHED...
L5 2 L4 AND TREAT?

=> dis l5 1-2 bib abs

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:284544 CAPLUS
DN 143:322280
TI Biological and chemical study of Rhamnus lycioides L. leaves growing in Egypt
AU El-Dondity, S. E.
CS Department of Pharmacognosy, Faculty of Pharmacy (boys), Al-Azhar University, Cairo, Egypt
SO Egyptian Journal of Biomedical Sciences (2004), 16, 527-539
CODEN: EJBSF3; ISSN: 1110-6379
PB Egyptian Society for Biotechnology
DT Journal
LA English
AB The L D50 of 70 % alc. extract of Rhamnus lycioides L. leaves was carried out to determine the safety margin of the leaves. A double-blind trial comparing different concns. of ointments prepared from 70 % alc. exts. of Rhamnus lycioides L. leaves with, standard therapy, flumethasone pivalate ointment and a placebo showed that, the exts. of Rhamnus lycioides L. leaves was effective in **treatment** of induced eczema in mice. A double-blind clin. trial comparing a 2% ointment prepared from 70 % alc. exts. of Rhamnus lycioides L. leaves with a 0.2 % flumethasone pivalate ointment and a placebo showed that, the 0.2% weight/weight of flumethasone pivalate ointment was better than 2% weight/weight Rhamnus lycioides L. leaves ointment but recurrence is larger in flumethasone pivalate ointment than Rhamnus lycioides L. leaves ointment. The results obtained with the extract were statistically comparable to those obtained with the corticoid therapy. Chemical study to isolation and identification of quercetin, and 2 new flavonol glycosides acetate esters viz., {**kaempferol**-3-O-[2,3,4,-tri-O-**acetyl**-α-L- **rhamnopyranosyl**-(1→3) - 2,4,- di-O- **acetyl**-α-L-

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rhamnopyranosyl-(1 → 6)]-β-D-galactopyranoside and
kaempferol-3-O-[3,4,-di-O-**acetyl**-α-L-
rhamnopyranosyl-(1 → 3) - 2,4,- di-O- **acetyl**
-α-L- **rhamnopyranosyl**-(1 → 6)]-β-D-
galactopyranoside}. This is also the first report for isolation of
quercetin from this species.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 USPATFULL on STN
AN 2002:105722 USPATFULL
TI Novel compositions derived from cranberry and grapefruit and therapeutic uses therefor
IN Leahy, Margaret M., Pocasset, MA, UNITED STATES
Starr, Martin, Plymouth, MA, UNITED STATES
Kurowska, Elzbieta, London, CANADA
Guthrie, Najla, London, CANADA
PI US 2002054924 A1 20020509
AI US 2001-835121 A1 20010413 (9)
PRAI US 2000-196886P 20000413 (60)
DT Utility
FS APPLICATION
LREP LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 2406
AB Novel compositions derived from grapefruit and cranberry are disclosed, as well as therapeutic uses for the compositions in **treating** or preventing cancer and hypercholesterolemia in a subject. The compositions are, in particular embodiments, derived from grapefruit essence oil, grapefruit peel oil, grapefruit peel, and decharacterized cranberry fruit.

=> s l3 and (alkoxy(a)rhamnopyranosyl)
L6 0 L3 AND (ALKOXY(A) RHAMNOPYRANOSYL)

=> dis hist

(FILE 'HOME' ENTERED AT 10:54:14 ON 29 NOV 2005)

FILE 'APOLLIT, BABS, CAPLUS, CBNB, CEN, CIN, COMPENDEX, DISSABS, EMA, IFIPAT, JICST-EPLUS, NTIS, PASCAL, PROMT, RAPRA, SCISEARCH, TEXTILETECH, USPATFULL, USPAT2, WPIFV, WPINDEX, WSCA, WTEXTILES, MEDLINE, BIOSIS, EMBASE' ENTERED AT 10:54:35 ON 29 NOV 2005
L1 268 S AFZELIN
L2 23 S L1 AND (ALKOXY OR ACETYL)
L3 16275 S KAEMPFEROL
L4 62 S L3 AND (ACETYL(S)RHAMNOPYRANOSYL)
L5 2 S L4 AND TREAT?
L6 0 S L3 AND (ALKOXY(A)RHAMNOPYRANOSYL)

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=> s l36 and l46
L47          0 FILE MEDLINE
L48          0 FILE BIOSIS
L49          0 FILE EMBASE
L50          3 FILE CAPLUS

TOTAL FOR ALL FILES
L51          3 L36 AND L46

=> d 1-3 ibib abs hitstr

L51  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:101479  CAPLUS
DOCUMENT NUMBER:          142:329195
TITLE:                    Identification of the first specific inhibitor
                          of p90 ribosomal S6 kinase (RSK) reveals an unexpected
                          role for RSK in cancer cell proliferation
AUTHOR(S):                Smith, Jeffrey A.; Poteet-Smith, Celeste E.; Xu,
                          Yaming; Errington, Timothy M.; Hecht, Sidney M.;
                          Lannigan, Deborah A.
CORPORATE SOURCE:         Center for Cell Signaling, University of Virginia,
                          Charlottesville, VA, USA
SOURCE:                   Cancer Research (2005), 65(3), 1027-1034
                          CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER:                American Association for Cancer Research
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   P90 ribosomal S6 kinase (RSK) is an important downstream effector of
     mitogen-activated protein kinase, but its biol. functions are not well
     understood.  The authors have now identified the first small-mol.,
     RSK-specific inhibitor, which they isolated from the tropical
     plant Forsteronia refracta.  The authors have named
     this novel inhibitor SL0101.  SL0101 shows remarkable
     specificity for RSK.  The major determinant of SL0101-binding specificity
     is the unique ATP-interacting sequence in the amino-terminal kinase domain
     of RSK.  SL0101 inhibits proliferation of the human breast
     cancer cell line MCF-7, producing a cell cycle block in G1 phase with an
     efficacy paralleling its ability to inhibit RSK in intact cells.
     RNA interference of RSK expression confirmed that RSK regulates MCF-7
     proliferation.  Interestingly, SL0101 does not alter proliferation of a
     normal human breast cell line MCF-10A, although SL0101 inhibits
     RSK in these cells.  RSK is overexpressed in .apprx. 50% of human breast
     cancer tissue samples, suggesting that regulation of RSK has been
     compromised.  Thus, RSK has an unexpected role in proliferation of
     transformed cells and may be a useful new target for chemotherapeutic
     agents.  SL0101 will provide a powerful new tool to dissect the mol.
     functions of RSK in cancer cells.
IT   77307-50-7
     RL: NPO (Natural product occurrence); PAC (Pharmacological activity); THU
     (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
        (identification of first specific inhibitor of p90 ribosomal
        S6 kinase (RSK) reveals an unexpected role for RSK in cancer cell
        proliferation)
RN   77307-50-7  CAPLUS
CN   4H-1-Benzopyran-4-one, 3-[(3,4-di-O-acetyl-6-deoxy-α-L-
     mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI)  (CA INDEX
     NAME)

Absolute stereochemistry.  Rotation (-).
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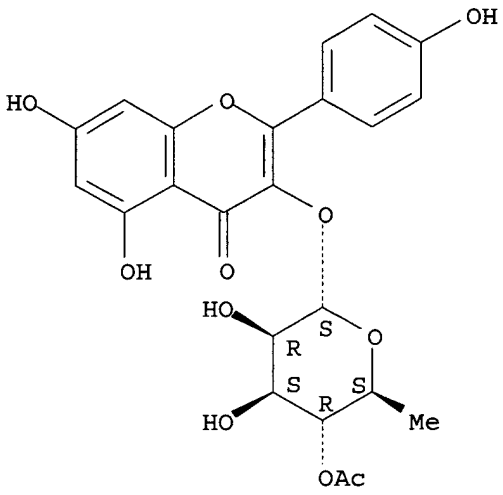


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=> s therap? or treat? or inhibit?
L28     4653890 FILE MEDLINE
L29     3541114 FILE BIOSIS
L30     4235684 FILE EMBASE
L31     4773546 FILE CAPLUS
 75% OF LIMIT FOR TOTAL ANSWERS REACHED
COMMAND INTERRUPTED
If this message appears repeatedly, please notify the Help Desk.
Enter "HELP STN" for information on contacting the nearest STN Help
Desk by telephone or via SEND in the STNMAIL file.

=> s l12 and (therap? or treat? or inhibit?)
L32         869 FILE MEDLINE
L33         782 FILE BIOSIS
L34        1208 FILE EMBASE
L35        3182 FILE CAPLUS

TOTAL FOR ALL FILES
L36        6041 L12 AND (THERAP? OR TREAT? OR INHIBIT?)

=> s rsk! and l36
L37           0 FILE MEDLINE
L38           0 FILE BIOSIS
L39           0 FILE EMBASE
L40           0 FILE CAPLUS

TOTAL FOR ALL FILES
L41           0 RSK! AND L36

=> s forsteronia refracta or zingiber zerumbet
L42          14 FILE MEDLINE
L43          46 FILE BIOSIS
L44          14 FILE EMBASE
L45          74 FILE CAPLUS

TOTAL FOR ALL FILES
L46         148 FORSTERONIA REFRACTA OR ZINGIBER ZERUMBET
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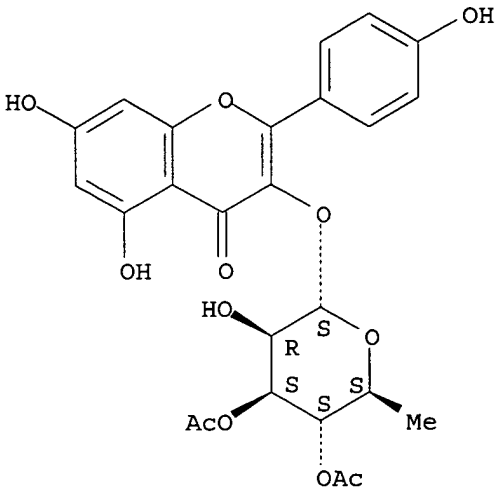
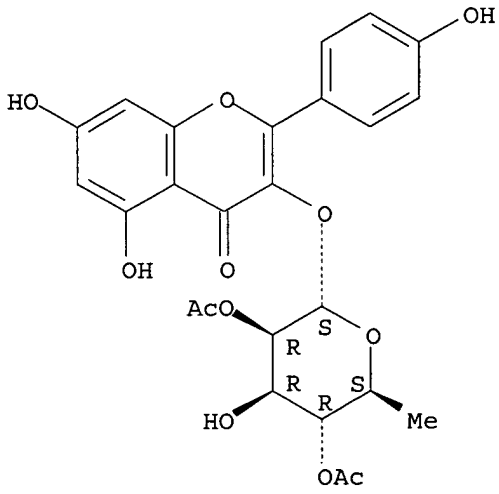
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86



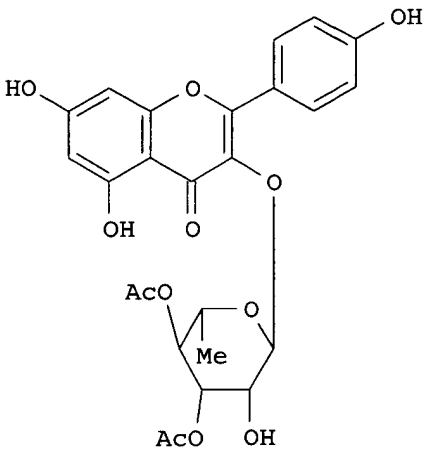
IT **133882-73-2P**, SL 0101-2 **135618-17-6P**, SL 0101-3
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(**Rsk** inhibitors and therapeutic uses)
RN 133882-73-2 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(2,4-di-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 135618-17-6 CAPLUS
CN 4H-1-Benzopyran-4-one, 3-[(4-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



I

AB The invention discloses compds. and **compns.** that have **Rsk**-specific inhibitory activity. Compds. of the invention include small mol. inhibitors, e.g. I. Synthetic procedures leading to I are described, as are isolation procedures from Forsteronia refracta. Other **Rsk**-specific inhibitors include e.g. antisense oligonucleotides. In addition, inhibition of **Rsk** by the compds. has been discovered to halt the proliferation of cancer cell lines while having little effect on the proliferation rate of normal cells. Therefore, the invention identifies **Rsk** as a target for therapeutic intervention in diseased states in which the disease or the symptoms can be ameliorated by inhibition of **Rsk** catalytic activity.

IT **77307-50-7P**, SL 0101-1
RL: DMA (Drug mechanism of action); NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(**Rsk** inhibitors and therapeutic uses)

RN 77307-50-7 CAPLUS

CN 4H-1-Benzopyran-4-one, 3-[(3,4-di-O-acetyl-6-deoxy-α-L-mannopyranosyl)oxy]-5,7-dihydroxy-2-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).